Capillary rarefaction in chronic kidney disease (CKD) (Cap-CKD): A survey on microvasculature and renal function in patients undergoing a nephrectomy

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Objectives: The main objective is to study renal tissue in relation to renal function before and after nephrectomy with a specific focus on microvascular structure and function. A second objective is to study renal microvascular alterations in...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational invasive

Summary

ID

NL-OMON46422

Source
ToetsingOnline

Brief title
Capillary rarefaction in chronic kidney disease (CKD): Cap-CKD

Condition

- Renal disorders (excl nephropathies)
- Vascular hypertensive disorders

Synonym
kidney failure; kidney disease

Research involving
Human

Sponsors and support

Primary sponsor: Pathologie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: capillary rarefaction, chronic kidney disease, kidney, microvasculature

Outcome measures

Primary outcome

Primary Objective:

The primary objective of the study is to assess the relationship between renal PTC density and renal function before and two years after surgery.

Secondary outcome

Secondary Objectives:

The secondary objectives of the study are to assess

a) the relationship between renal PTC density and systemic capillary density and microvascular function in patients with and without CKD at nephrectomy and after two years.

b) the relationship between renal PTC density and histological and molecular damage (e.g. IF/TA, inflammation, angiogenic profiling, MSI) in renal tissue in patients with and without CKD at nephrectomy and after two years.

c) the relationship between renal PTC density and renal function in relation to known cardiovascular risk factors such as demographic variables (age, gender), clinical variables (renal function, hypertension. glucose intolerance, mineral metabolism, BMI), and medical history (smoking history, medication use, birth weight).

Study description

Background summary

Rationale:
Chronic kidney disease (CKD) affects 10-15% of the general population and is an independent risk factor for cardiovascular disease. Symptoms of CKD become noticeable at a late stage, and better insight into the underlying pathophysiology is needed to enable early disease detection. From the field of renal transplantation we know that histological damage in kidney tissue precedes renal function decline, and recently we and others have found an important role for loss of microvascular stability (i.e. capillary rarefaction) as an underlying pathophysiological mechanism. We would like to translate these findings to the general population in relation to the development of CKD. As renal tissue cannot be routinely obtained, we aim to study nephrectomy specimens for pathological alterations and capillary rarefaction. In order to relate these findings to CKD and vascular parameters we will study patients who are well phenotyped for these specific parameters before and after nephrectomy for a renal cell carcinoma.

Study objective

Objectives:
The main objective is to study renal tissue in relation to renal function before and after nephrectomy with a specific focus on microvascular structure and function. A second objective is to study renal microvascular alterations in relation to systemic microvascular and macrovascular dysfunction.

Study design

Study design:
This is a prospective observational study, with a follow-up duration of 24 months. In this study, renal function and vascular parameters will be assessed in relation to renal tissue examination in 281 patients who undergo a nephrectomy for a suspected renal cell carcinoma.

Intervention:
This is a non-interventional study.

Main study parameters/endpoints:
This will comprise a selection of minimally invasive measurements and laboratory parameters, as well as medical history and physical examination. We will include:
Medical history: detailed, i.e. including smoking history, birth weight, use of medication

Physical examination: 24 hour blood pressure measurement, body mass index, and waist circumference will be taken before nephrectomy and two years after nephrectomy.
Renal function: eGFR will be calculated using the CKD-epi and the Cockcroft Gault formula using gender, race, age, weight and serum creatinine (see below). This will be done before the nephrectomy, 4-8 weeks after the nephrectomy, and 2 years after the nephrectomy.
Serum and plasma collection and analysis: Sodium, potassium, calcium, phosphate, urea, creatinin, albumin, cholesterol, glucose, hemoglobn, tCO2, PTH and uric acid. Furthermore, serum and plasma will be stored for future analyses.
Urine collection and analysis: Three 24 hour urine collections (volume, total protein, microalbuminuria, creatinin, phosphate, urea, sodium) and one morning urine sample (urinary sediment) before, 4-8 weeks and 2 years after nephrectomy. Furthermore, urine samples will be stored for future analyses.
Vascular function measurements: Systemic capillary function will be measured in the skin using intravital microscopy with and without arterial and venous occlusion. Furthermore, skin microvascular function will be studied using laser-doppler flowmetry. Finally, pulse wave velocity will be determined.
Renal tissue analysis: Renal tissue adjacent to the tumour will be sampled for histological and molecular analysis with e.g. immunohistochemistry, morphometry, electron microscopy (EM), angiogenic profiling, mass spectrometry imaging (MSI) and flow cytometry (FACS).

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
In this study, only minimally invasive techniques will be performed using mobile equipment, which pose a minimal burden to the patient. Blood sampling will coincide as much as possible with regular blood takings for clinical purposes before nephrectomy. Before the nephrectomy an additional visit to the out-patient clinic is necessary. The follow up renal function measurements, several weeks and two years after the nephrectomy, will coincide with the routine follow-up visit of the patient with the urologist to diminish burden for the patient. Renal tissue adjacent to the tumour will be sampled during routine pathological analysis of the nephrectomy specimen. The study will not have direct benefit for the participants. The study can only be performed within this specific patient group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients who undergo a nephrectomy for a suspected renal cell carcinoma and who are 18 years or older and are able to read and write.

Exclusion criteria

none

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	281
Type:	Anticipated

Ethics review

Approved WMO Date:	12-12-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65499.068.18